REMARKS

Receipt of the Office Action mailed July 14, 2003 is acknowledged. Applicants respectfully request reconsideration of the present application in view of the reasons that follow.

Claims 1-18 and 20-40 are now pending in this application. Claims 33-40 have been withdrawn from consideration, and claims 1-18 and 20-32 are currently presented for consideration. Claims 1-18 and 20-32 stand rejected under 35 USC § 103(a) as allegedly being unpatentable over Bellhouse et al., United States Patent No. 5,630,796 (the "'796 patent") in view of Gerstel et al., United States Patent No. 3,964,482 (the "'482 patent"). Claims 1-18 and 20-32 also stand rejected under 35 USC § 103(a) as allegedly being unpatentable over the '482 patent in view of the '796 patent. Applicants respectfully traverse these rejections. Applicants note with appreciation that the Examiner has withdrawn all other rejections.

35 USC § 103(a) – '796 patent in view of '482 patent

Claims 1-18 and 20-32 stand rejected under 35 USC § 103(a) as allegedly being unpatentable over the '796 patent in view of the '482 patent. In the '796 patent, the Examiner refers to the abstract, col. 2, ll. 30-37, col. 4, ll. 1-23 & 40-55, col. 8, ll. 17-20, and col. 10, example 2 as disclosing a needleless syringe for effective transdermal delivery of particles containing a therapeutic agent such as viruses or proteins (antigen), insulin with a carrier (adjuvant) or a placebo. The Examiner acknowledges that the '796 patent does not disclose topically positioning a transdermal drug delivery device or a first occlusive dressing over the area of the skin or mucosa as claimed.

In the '482 patent, the Examiner refers to the abstract, col. 3, ll. 15-18 & 24-29, col. 4, ll. 46-60, and col. 7, ll. 29-31 as disclosing a drug delivery device for percutaneously administering a drug, where the device comprises a plurality of projections to penetrate the stratum corneum of the skin for delivering the drug from a drug reservoir to produce local or systemic pharmaceutical effect. The Examiner also states that the reference teaches puncturing or scraping the stratum

corneum before application of the drug for enhancing drug administration percutaneously to achieve local or systemic therapy for prolonged periods of time.

The Examiner then concludes that it would have been obvious to one having ordinary skill in the art to provide a method for administering a therapeutic agent to the skin or mucosa comprising applying particles to the skin by the needleless syringe as disclosed in the '796 patent and then applying a transdermal device containing a drug as disclosed in the '482 patent motivated by the teaching that puncturing or scraping the stratum corneum before application of the transdermal drug delivery device enhances the percutaneous drug administration to achieve local or systemic therapy for prolonged periods of time, with a reasonable expectation of having a method to administer drugs through the skin or mucosa for a prolonged period of time with success.

Applicants respectfully submit that the Examiner has failed to establish *prima facie* obviousness over the proposed combination of the '796 patent and the '482 patent. The '796 patent and the '482 patent do not disclose or teach all of the limitations of the presently claimed invention. In addition, as will be seen below, one of skill in the art would not have combined the two separate and distinct methods disclosed in the '796 patent and the '482 patent. Moreover, the '796 patent and the '482 patent do not provide the requisite motivation to combine the methods disclosed in the references, nor do they convey a reasonable expectation of success in making the claimed invention. The combination suggested by the Examiner is arbitrary and stems from improper hindsight.

As the Examiner acknowledges, the '796 patent does not disclose topically positioning a transdermal drug delivery device or a first occlusive dressing over the area of the skin or mucosa. In addition, the '796 patent does not disclose the use of particles that contain no therapeutic agent, *i.e.*, placebo particles. While the '796 patent discloses the use of "gas only (no powder) . . . as a placebo" for the control sample in Example 2, it does not disclose a method of using the disclosed device to administer strictly placebo *particles*. In addition, the '796 patent does not disclose administering placebo particles as a step in a method to administer a

therapeutic agent. The gas-only placebo administration disclosed in Example 2 not only fails to administer particles, but it also fails to administer a therapeutic agent. As will become evident below, the '482 patent does not remedy the defects in the disclosure of the '796 patent.

The '482 patent does not disclose accelerating particles into, across or both into and across the area of skin or mucosa, wherein the particles are accelerated toward the skin or mucosa using a needless syringe device, as claimed. Nor does the '482 patent disclose accelerating *placebo* particles or positioning an occlusive dressing over the area of skin or mucosa. Further, Applicants respectfully submit that the Examiner's characterization of the '482 patent is misleading. The Examiner states that the reference teaches puncturing the stratum corneum before application of the drug for enhancing the drug administration percutaneously; however, upon a careful reading, it becomes clear that the patent teaches that the puncturing projections must maintain contact with the skin layers under the stratum corneum in order to effectively administer the drug. See '482 patent, col. 4, ll. 39-44. In other words, the puncturing occurs as part of the topical positioning of the transdermal drug delivery device and not before the topical positioning of the device as claimed in the instant application.

The Examiner also asserts that the '482 patent teaches scratching the stratum corneum before application of the drug for enhancing the drug administration percutaneously. However, the '482 patent does not teach at what time the puncturing projections scrape the stratum corneum, and, particularly important, it does not teach pretreating the skin by scraping the stratum corneum in order to enhance administration of a therapeutic drug. The disclosure of the '482 patent is unlike the claimed invention for several reasons, but particularly because the particles in the claimed invention are accelerated into, across or both into and across the area of skin or mucosa before the topical positioning of a first transdermal drug delivery device and there are no puncturing projections maintaining contact with the skin layers under the stratum corneum.

Applicants further submit that the '482 patent does not provide any motivation to arrive at the claimed invention. The '482 patent does not suggest to one of skill in the art to accelerate

particles into, across or both into and across the area of skin or mucosa, wherein the particles are accelerated toward the skin or mucosa using a needless syringe device and then topically position a first transdermal drug delivery device or a first occlusive dressing over the area of skin or mucosa, as claimed. Each patent, the '796 patent and the '482 patent, discloses a complete and separate method for administering a therapeutic agent. In other words, if one were to treat the skin with particles containing a therapeutic agent as disclosed in the '796 patent, the subsequent treatment with the device disclosed in the '482 patent would be redundant. Accordingly, one of skill in the art would not combine a method that effectively delivers a drug with a second method that also effectively delivers a drug, absent a promise of enhanced delivery. However, there would be no reasonable expectation of successfully enhancing the drug delivery with the proposed combination. The initial administration of the particles containing a therapeutic agent according to the '796 patent would not enhance the administration of the therapeutic agent by the device disclosed in the '482 patent. This is because the puncturing projections that are part of the device disclosed in the '482 patent reach directly through the stratum corneum to the lower layers of the skin for administration, therefore bypassing any benefit derived from the administration of the particles. As a result, one of skill in the art would not have been motivated to combine these two patents to arrive at the claimed invention based on a desire to achieve enhanced percutaneous drug administration.

Furthermore, the '796 patent teaches away from the combination suggested by the Examiner. The '796 patent discloses the invention as being "useful for routine delivery of drugs, such as insulin . . ., and could be of use in mass immunisation programs, or for the delivery of slow release drugs such as pain killers and contraceptives." '796 patent, col. 1, ll. 45-48. The '796 patent goes on to note that the "main advantages which flow from the invention include no needle and less pain; no risk of infection; delivery of drugs in natural, solid form; quicker and safer to use than liquid drug, by syringe and needle; and no sharps to dispose of." '796 patent, col. 1, ll. 61-65. Accordingly, it is clear that the '796 patent is useful for the mere routine delivery of drugs, not a multi-step drug delivery technique where different drug delivery technologies are used to custom tailor drug delivery profiles as claimed. Second, the '796 patent

clearly discloses that delivery of drugs using the disclosed device does not result in bleeding or pain. The '482 patent, on the other hand, discloses a device that utilizes "puncturing projections" to puncture the stratum corneum and then deliver the drug to the skin layers below the stratum corneum. '482 patent, col. 7, ll. 23-32. As such, contrary to the Office's assertions, one of skill in the art would not be motivated to combine a pain free method of administering drugs with a method that requires projections to puncture and maintain contact with the lower layers of skin in order to administer the drugs. Therefore, the '796 patent does not disclose or suggest the method as set forth in claim 1. There is nothing in the '482 patent that would cure the deficiencies in the '796 patent. As such, claim 1 is patentable over this combination of references. Since claims 2-18 and 20-32 are dependent from claim 1, for at least this reason claims 2-18 and 20-32 are patentable over the prior art of record.

35 USC § 103(a) – '482 patent in view of '796 patent

Claims 1-18 and 20-32 also stand rejected under 35 USC § 103(a) as allegedly being unpatentable over the '482 patent in view of the '796 patent. The Examiner states that it would have been obvious to one having ordinary skill in the art to provide a method for administering a therapeutic agent across the skin as disclosed by the '482 patent and replace the projections that puncture the skin with the needleless particle injection as disclosed in the '796 patent, motivated by the teaching of the '796 patent that the needleless injection of the particles using the needleless injector provides less pain, safe, quick, no risk of infection, delivery of the drug in natural solid form, with reasonable expectation of having a method to administer drugs through the skin or mucosa for a prolonged period of time with success.

As discussed in the previous section, the '482 patent and the '796 patent do not disclose or teach all of the limitations of the presently claimed invention. Moreover, for the reasons stated above, the combination suggested by the Examiner would not have rendered the pending claims obvious at the time the invention was made to a person having ordinary skill in the art.

Applicants further submit that the '796 patent does not provide the requisite motivation to combine the methods disclosed in the references. Particularly, applicants assert that one of skill in the art would not have been motivated to replace the puncturing projections disclosed in the '482 patent with a needleless syringe administration of particles containing a therapeutic agent disclosed in the '796 patent as suggested by the Examiner. In addition, the '796 patent does not convey a reasonable expectation of success in making the claimed invention. There would be no reasonable expectation of successfully enhancing the drug delivery with the proposed combination. If one of skill in the art were to administer particles with the device disclosed in the '796 patent and then, if one were to remove the projection part of the device disclosed in the '482 patent as suggested by the Examiner, he or she would be left with a reservoir and no means of applying the therapeutic agent from the reservoir to the skin. The Examiner acknowledged in the Office Action that the device disclosed in the '482 patent comprises only two parts, "one part comprising the projection and the second part is the drug reservoir (col. 4, lines 46-50)." Removing the projection part would leave one of skill in the art with the option of pouring the drug over the skin or mucosa. Therefore, this combination would not inspire a reasonable expectation of success.

Therefore, the '482 patent does not disclose or suggest the method as set forth in claim 1. There is nothing in the '796 patent that would cure the deficiencies in the '482 patent. As such, claim 1 is patentable over this combination of references. Since claims 2-18 and 20-32 are dependent from claim 1, for at least this reason claims 2-18 and 20-32 are patentable over the prior art of record. Accordingly, applicants respectfully request that the two obviousness rejections be reconsidered and withdrawn.

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, applicants hereby petition for such extension under 37 C.F.R. § 1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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